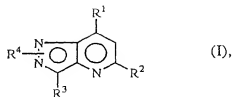


Claims

1. Use of compounds of formula (I)



including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

R¹ is C₁₋₆alkyl, NR⁵R⁶, OR⁶ or SR⁶;

R² is C₁₋₆alkyl, C₁₋₆alkyloxy, or C₁₋₆alkylthio;

R³ is Ar¹ or Het¹;

R⁴ is hydrogen or C₁₋₆alkyl;

R⁵ is hydrogen, C₁₋₆alkyl, mono- or di(C₃₋₆cycloalkyl)methyl, C₃₋₆cycloalkyl, C₃₋₆alkenyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyloxyC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl;

R⁶ is C₁₋₆alkyl, mono- or di(C₃₋₆cycloalkyl)methyl, Ar²C₁₋₆alkyl, Ar²oxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₃₋₆alkenyl, thienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C₁₋₆alkylthioC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, di(C₁₋₆alkyl)amino, or C₁₋₆alkylcarbonylC₁₋₆alkyl;

or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl, morpholinyl, or thiomorpholinyl group, optionally substituted with 1 or 2 substituents each independently selected from C₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl;

Ar¹ is phenyl; naphthyl; or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁₋₆alkyl, trifluoromethyl, hydroxy, cyano, C₁₋₆alkyloxy, benzyl, benzyloxy, C₁₋₆alkylthio, nitro, amino and mono- or di(C₁₋₆alkyl)amino;

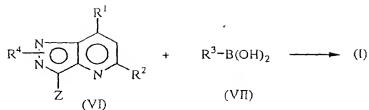
Het¹ is pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁₋₆alkyl, trifluoromethyl, hydroxy, cyano, C₁₋₆alkyloxy, benzyloxy, C₁₋₆alkylthio, nitro, amino, and mono- or di(C₁₋₆alkyl)amino; and

Ar² is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, di(C₁₋₆alkyl)aminoC₁₋₆alkyl, or trifluoromethyl; or pyridinyl; for the manufacture of a medicament for treating physiological conditions or disorders arising from the hypersecretion of corticotropin-releasing factor (CRF).

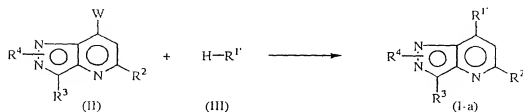
2. Use of a compound according to claim 1 wherein R¹ is NR⁵R⁶ wherein R⁵ is hydrogen or C₁₋₆alkyl; and R⁶ is C₁₋₆alkyl or C₃₋₆cycloalkylmethyl; or R¹ is OR⁶ or SR⁶ wherein R⁶ is C₁₋₆alkyl; R² is C₁₋₆alkyl; R³ is a phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkyloxy or halo; or R³ is a pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, amino, nitro, trifluoromethyl, mono- or di(C₁₋₆alkyl)amino, or C₁₋₆alkyl; and R⁴ is hydrogen or C₁₋₆alkyl.

3. A compound of formula (I-1) wherein R¹ to R⁴ are defined as in claim 1 and wherein at least R¹ is C₁₋₆alkyl; OR⁶; SR⁶; or NR⁵R⁶ wherein R⁵ is mono- or di(C₃₋₆cycloalkyl)methyl, C₃₋₆cycloalkyl, C₃₋₆alkenyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyloxyC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl, and R⁶ is mono- or di(C₃₋₆cycloalkyl)methyl, Ar²C₁₋₆alkyl, Ar²oxyC₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkyl, C₃₋₆alkenyl, thienylmethyl, furanymethyl, tetrahydrofuranymethyl, C₁₋₆alkylthioC₁₋₆alkyl, C₁₋₆alkylcarbonylC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, or di(C₁₋₆alkyl)amino; or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl; or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl; or at least R³ is Het¹ or Ar¹ wherein Ar¹ is naphthyl; or phenyl substituted with 3 substituents each independently selected from halo, C₁₋₆alkyl, trifluoromethyl, hydroxy, cyano, C₁₋₆alkyloxy, benzyl, benzyloxy, C₁₋₆alkylthio, nitro, amino and mono- or di(C₁₋₆alkyl)amino.

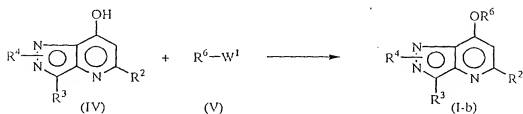
4. A compound according to claim 3 wherein R^1 is a radical of formula NR^5R^6 wherein R^5 is mono- or di(C_{3-6} cycloalkyl)-methyl, C_{3-6} cycloalkyl, C_{3-6} alkenyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyloxy C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino- C_{1-6} alkyl or C_{1-6} alkyloxy C_{1-6} alkyl, and R^6 is mono- or di(C_{3-6} cycloalkyl)methyl, Ar² C_{1-6} alkyl, Ar²oxy C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy C_{1-6} alkyl, C_{3-6} alkenyl, thienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C_{1-6} alkylthio C_{1-6} alkyl, C_{1-6} alkylcarbonyl C_{1-6} alkyl, mono- or di(C_{1-6} alkyl)amino C_{1-6} alkyl, or di(C_{1-6} alkyl)amino.
- 10 5. A compound according to claim 3 wherein R^1 is a radical of formula NR^5R^6 wherein R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C_{1-6} alkyl or C_{1-6} alkyloxy C_{1-6} alkyl; or R^5 and R^6 taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C_{1-6} alkyl or C_{1-6} alkyloxy C_{1-6} alkyl.
- 15 6. A compound according to claim 3 wherein R^3 is Het¹ or Ar¹ wherein Ar¹ is naphthyl; or phenyl substituted with 3 substituents each independently selected from halo, C_{1-6} alkyl, trifluoromethyl, hydroxy, cyano, C_{1-6} alkyloxy, benzyl, benzyloxy, C_{1-6} alkylthio, nitro, amino or mono- or di(C_{1-6} alkyl)amino.
- 20 7. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6.
- 25 8. A process for preparing a composition as claimed in claim 7 wherein a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6 is intimately mixed with a pharmaceutically acceptable carrier.
- 30 9. A compound according to any one of claims 3 to 6 for use as a medicine.
- 35 10. A process of preparing a compound of formula (I-1) as claimed in claim 3 wherein a) intermediates of formula (VI) are reacted with intermediates of formula (VII) under Suzuki coupling conditions;



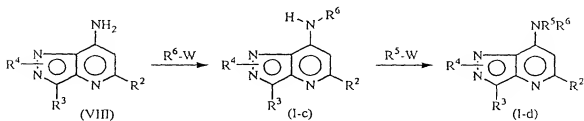
b) an intermediate of formula (II) is reacted with an intermediate of formula (III), wherein R^{1'} has the meaning of R¹ other than C₁₋₆alkyl, thereby yielding compounds of formula (I-a);



c) an intermediate of formula (IV) is *O*-alkylated with an intermediate of formula (V) in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-b), defined as compounds of formula (I) wherein R¹ is OR⁶,



d) an intermediate of formula (VIII) is *N*-alkylated with an intermediate of formula R⁶-W in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-c), which can be further *N*-alkylated with an intermediate of formula R⁵-W



wherein in the above reaction schemes the radicals R^1 to R^6 , are as defined in claim 1, Z is bromo or iodo and W and W^1 are appropriate leaving groups;

- 5 or, if desired, compounds of formula (I) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (I) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.